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(54) Title: NOVEL METHODS FOR THE IDENTIFICATION OF LIGAND AND TARGET BIOMOLECULES

(57) Abstract

The invention provides for methods for identification of biologically active biomolecules. In one aspect, a biologically active biomolecule such as RNA or a peptide is identified by incorporating random nucleotide sequences in a scaffold constituted by an enzyme activity modulator, transforming substantially identical host cells with the construct obtained thereby and screening the transformed cells to identify those where a preselected phenotypic trait has been altered. The randomized DNA is subsequently isolated from the phenotypically altered cells and the peptide and/or RNA encoded by the random sequence is determined. In turn, interaction partners which are putative drug targets are identified and isolated by use of the peptide and/or RNA as part of affinity reagents. A preferred scaffold is derived from the potato inhibitor I family of protease inhibitors and exemplified is the barley chymotrypsin inhibitor 2A (CI–2A). Another aspect relates to the identification of novel enzyme inhibitors by using substantially the same approach, but screening specifically for changes in target enzyme activity. Also disclosed are methods of producing the relevant transformation and expression vectors as well as methods for identifying lead compounds and drug targets for use in drug development. Finally, the invention also includes within its scope a method for the preparation of a medicinal product.